201-14931

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12/18/2003 04:14 PM

To: Rtk Chem@EPA, NCIC OPPT@EPA
cc:
Subject: Test Plan and Robust Summary Submission

Great Lakes Chemical Corporation (GLCC) is pleased to submit, attached below, the Test Plan, Test Plan Matrix, and Robust Summaries as part of the HPV Challenge Program for the following chemical:

Benzene, ethenyl-, aryl-bromo derivatives-CAS # 125904-11-2

GLCC understands there will be a 120-day review period for the Test Plan and that all comments received by the EPA will be forwarded to Great Lakes.

Please feel free to contact me (765-497-6114) with any questions you might have concerning this submission.

Sincerely,

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E-mail: rhenrich@glcc.com DBS HPV IUCLID Summary 12 18 2003.c DBS HPV TEST PLAN2 12 18 03.dc

TEST PLAN FOR BENZENE, ETHENYL-, ARYL-BROMO DERIVS. (CAS NO. 125904-11-2)

OVERVIEW

Great Lakes Chemical Corporation agrees to sponsor Benzene, ethenyl-, aryl-bromo derives. (CAS NO. 125904-11-2) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. The company hereby submits a test plan for this substance. It is the intent of the sponsoring company to use existing data combined with new studies specified in the test plan to fulfill the Screening Information Set (SIDS) endpoints for environmental fate, ecotoxicity and human health effects.

TEST PLAN

CHEM
Benzene, ethenyl-, ar-bromo derivs.

CAS #
125904-11-2

Study Type	Data Available	Data Acceptable	Testing Required
Physical/Chemical Properties			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
Environmental Fate			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Biodegradation	Y	Y	N
Fugacity	Y	Y	N
Ecotoxicity			
Acute Toxicity to Fish	N	N	Y
Acute Toxicity to Aquatic Invert.	N	N	Y
Toxicity to Aquatic Plants	N	N	Y
Human Health Effects Toxicity			
Acute Toxicity	Y	Y	N
General Toxicity (repeated dose)	Y	Y	N
In vitro - Genetic Toxicity Mutation	Y	Y	N
In vitro – Genetic Toxicity Chromosomal Aberrations	Y	Y	N
Reproductive Toxicity	Y	Y	N
Developmental Toxicity	Y	Y	N

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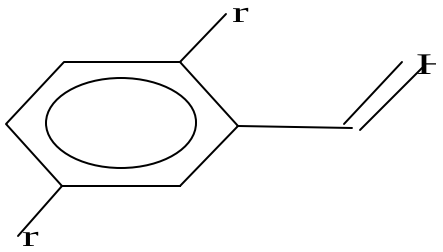
1. Introduction

Great Lakes Chemical Corporation submits this test plan for Benzene, ethenyl-, aryl-bromo derives. (CAS NO. 125904-11-2) for hazard review under the Environmental Protection Agency High Production Volume Chemical Program. The technical contact at this company is:

Richard Henrich
Great Lakes Chemical Corporation
West Lafayette, IN 47906
Phone (765) 497-6114

2. Designation of Test Substance

The test substance presented in this test plan is Benzene, ethenyl-, aryl-bromo derives. (CAS NO. 125904-11-2). The chemical structure is as follows:



This chemical is also known as: Dibromostyrene; DBS; CN-19; Step III; Brominated Styrene

The chemical is also sold under the trade names Great Lakes DBS-64, Great Lakes DBS, and Great Lakes PDBS-80.

The primary use of this chemical is incorporation in engineering thermoplastics as a flame retardant. Typically the material is polymerized then added to the plastic in such a way that extraction is very unlikely.

3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

4. Discussion of Available Test Information

4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 1.

Table 1. Chemical/physical properties of Dibromostyrene

Endpoint	Value
Melting point (° C)	-37
Boiling point (° C)	95
Vapor pressure (mmHg at 25° C)	0.075
Partition coefficient (Log Pow or Kow)	4.43
Water solubility (mg/l at 20 ° C)	6.91

4.1.1 Melting Point

A melting point of -37° C is an estimated value based on extrapolation from the viscosity test data. The viscosity of the test substance rapidly increases in the range of temperatures from -18 to - 23° C.

4.1.2 Boiling Point

The boiling point of 95 °C was determined in Great Lakes Chemical Corp. Department of Research and Development.

4.1.3 Vapor Pressure

The vapor pressure of the test substance was determined in Great Lakes Chemical Corp. Department of Research and Development.

4.1.4 Octanol/Water Partition Coefficient

A log Pow of 4.43 was measured (Wildlife International, 2003) according to OECD guideline 107, "Partition Coefficient (n-octanol/water), Flask-shaking method".

4.1.5 Water Solubility

A measured value of 6.91mg/L (Wildlife International, 2003) was obtained according to the OECD Guideline 105 "Water Solubility".

4.1.6 Summary/Test Plan for Physical Properties

The physical properties of dibromostyrene have been adequately assessed and no further testing is needed.

4.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 2.

Table 2. Environmental fate parameters for Dibromostyrene.

Endpoint	Value
Photolysis[b] (Atmospheric $T_{1/2}$)[b]	0.402 days
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)[b] (Atmospheric $T_{1/2}$)[b]	27 x 10^{-12} cm^3/molecule-sec 0.402 days
Stability in Water[a]	½life 39 - 59 days at pH 7
Biodegradation[b]	Not readily biodegraded
Henry's Law Constant[b]	0.00044 atm/m^3
Log Koc[a]	3.79
Environmental transport (Fugacity Level III mass percentages)[b]	Air = 0.616 Water = 16.2 Soil = 73.2 Sediment = 10

[a] Measured value
[b] Estimated using EPIWIN v3.11

4.2.1 Photodegradation

A hydroxyl radical-induced photodegradation rate constant of ca. 27 x 10^{-12} cm^3/molecule-sec has been estimated using EPIWIN (v3.11). The same program estimates a half-life of 4.8 hours for photodegradation. The strictly limited volatility of the test substance suggests that atmospheric photodegradation is not an important degradative pathway.

4.2.2 Stability in Water

The stability of dibromostyrene in water as a function of pH was measured by Wildlife International 2003. Dibromostyrene was determined to be hydrolytically stable at 19 degrees C, pH 4 and 7, but was marginally hydrolytically unstable at pH 9 (t1/2 = 177 days). At 25 degrees C, dibromostyrene degraded at all pH levels half-life ranged from 39-59 days.

4.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using EPIWIN v3.11. The results indicate that the test substance will partition preferentially to soil, water, and sediment. A calculated Henry's Law Constant of 4.88 x 10^{-4} atm-m^3/mol suggests that the test substance will not rapidly volatilize from water. Volatilization from soil or sediment is also strictly limited. A water soil partition constant (Koc) of 6166 has been estimated using EPIWIN PCKOC. This high value indicates that the test substance possesses poor soil mobility.

4.3.4 Biodegradation

EPIWIN v3.11 Level III Fugacity Model has predicted that dibromostyrene is expected to be found predominantly in soil and its persistence estimate is based on its transformation in this medium. Its half-life in soil is expected to be ca. 75 days. The overall persistence takes into account both a chemical's media-specific half-life as well as its rate of transport into and out of that compartment. The overall persistence of dibromostyrene is predicted to be ca. 49 days using the default emission scenario of the Level III multimedia model.

4.3.5 Bioaccumulation

The estimated bioconcentration factor (BCF) of dibromostyrene is 790 (EPIWIN v3.11). This value does not exceed the EPA bioconcentration criteria, therefore, it is not expected to bioaccumulate in the food chain.

4.3.6 Summary/Test Plan for Environmental Fate Parameters

Dibromostyrene is not expected to biodegrade rapidly and is expected to partition primarily to soil with little to no potential for significant mobility. It is not expected to bioaccumulate or biomagnify based on the EPIWIN model. Sufficient environmental fate information is available to adequately characterize environmental fate endpoints for screening purposes. No additional testing is necessary.

4.3 Ecotoxicity

4.3.1 Acute Toxicity to Fish

No data are available.

4.3.2 Acute Toxicity to Aquatic Invertebrates

No data are available.

4.3.3 Acute Toxicity to Aquatic Plants

No data are available.

4.3.4. Summary/Test Plan for Ecotoxicity

No ecotoxicity data are available for dibromostyrene. As the test plan indicates, acute toxicity studies in fish, daphnia, and algae will be conducted in order to better characterize the ecotoxicological data for dibromostyrene.

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

The acute oral toxicity of dibromostyrene has been characterized by WIL Research Laboratories (1983). The calculated LD50 from this study was 5.69 g/kg for males, 6.9 g/kg for females, and 6.33 g/kg combined. The acute oral toxicity of this compound is therefore considered to be very low. The acute inhalation toxicity of dibromostyrene was also assessed (Raltech Scientific Services, 1981) in a DOT Class B poison test. In this study, the LC 50 of dibromostyrene was determined to be > 3.1 mg/L. Thus, the acute inhalation toxicity potential of this compound is also very low. Finally, the acute dermal toxicity of dibromostyrene was determined by WIL Research Laboratories (1983). In this study the acute dermal LD50 was determined to be > 2000 mg/kg (WIL Research, 1983), therefore, the dermal toxicity of dibromostyrene is very low as well.

4.4.2 Repeated Dose Mammalian Toxicity

A 28-day range-finding oral gavage study of dibromostyrene revealed no effects on survival or other observed parameters at doses of 1, 10, 50, or 100 mg/kg/day (WIL Research Laboratories, Inc., 1987). Therefore, a 90-day repeated dose study with a 4-week recovery period was conducted by oral gavage with dibromostyrene at doses of 130, 300, 700, or 1600 mg/kg/day by WIL Research Laboratories, 1989. Hematological and metabolic effects were observed at doses of 300 mg/kg and higher. The NOAEL for systemic toxicity of dibromostyrene was determined to be 130 mg/kg bw.

4.4.3 Genetic Toxicity

4.4.3.1 Mutagenicity

Dibromostyrene has been tested for mutagenicity in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 as well as in the CHO/HGPRT mammalian cell gene mutation assay in the absence and presence of a metabolic activation system Results of both studies were negative (Litton Bionetics, Inc., 1982 and Microbiological Associates, Inc., 1987). This material was also evaluated in the unscheduled DNA synthesis assay in rat primary hepatocytes with and without metabolic activation. Dibromostyrene did not induce a significant increase in the number of net nuclear grain counts at any dose level, (Microbiological Associates, Inc., 1987).

4.4.3.2 Chromosomal aberration

Four chromosomal aberration studies in Chinese hamster ovary cells have been conducted with and without metabolic activation (Microbiologicat Associates, Inc., 1987; Pharmakon Research International, Inc., 1987; Pharmakon Research International, Inc., 1987; and Pharmakon Research International, 1987). The first study which included concentrations of 0.005, 0.01, 0.02, and 0.04 µL/mL gave an "ambiguous" result with and without metabolic activation. In the following three studies, all conducted at concentrations between 1 to 90 µg/mL, the material was found to be negative in its ability to induce chromosome aberrations (clastogenicity). These studies were all conducted over a 4-month time period, therefore it is unlikely that the formulations were significantly different to account for the "ambiguous" outlier. The

overwhelming body of literature for this endpoint indicates that dibromostyrene does not possess the potential to induce chromosomal aberrations.

4.4.4 Reproductive Toxicity

A two-generation reproduction study was conducted in rats with dibromostyrene administered by oral gavage at doses of 100, 400, or 1600 mg/kg/day (WIL Research Laboratories, 1987). A slight effect on fertility was observed among the F1 males at 1600 mg/kg (decreased mean testes weights). No other effects on reproductive parameters were observed in either the F1 or F0 generations. The NOAEL for reproductive toxicity was concluded to be 400 mg/kg/day. Neonatal toxicity was observed among pups in the 400 or 1600 mg/kg/day dose groups in both the F1 and F2 generations. These effects included slightly (not statistically significant) decreased litter size, decreased pup viability, changes in the clinical condition of the pups and decreased pup body weights. The NOAEL for neonatal toxicity was 100 mg/kg/day. Parental toxicity was apparent in the 400 and 1600 mg/kg/day treated groups. Based on renal and liver effects, the NOAEL for adults was determined to be < 100 mg/kg/day.

4.4.5 Developmental Toxicity

There are developmental toxicity studies for dibromostyrene in rats and rabbits. In rabbits, dibromostyrene was administered by oral gavage to pregnant dams at doses of 25, 75, 150, or 350 mg/kg/day on gestation days 6-18 (WIL Research Laboratories, 1993). Maternal toxicity was evident at 350 mg/kg/day and included mortality, clinical signs, body weight loss, and decreased food consumption. No fetal toxicity was observed at any dose. Therefore, the NOAEL for maternal toxicity was 150 mg/kg/day and 350 mg/kg/day for fetal toxicity. In rats, pregnant dams were administered 100, 400, 800, or 1600 mg/kg/day by oral gavage on gestation days 6-15 (WIL Research Laboratories, 1993). Maternal toxicity (reduced body weight gains and food consumption)was noted at all dose levels. Developmental toxicity was observed at 400 mg/kg/day and higher and included developmental variations such as unossified ribs and sternebrae. The NOAEL for maternal toxicity was < 100 mg/kg bw and for developmental toxicity it was 100 mg/kg bw.

4.5 Additional Data

4.5.1 Skin and Eye Irritation

The primary dermal and eye irritation for dibromostyrene has also been determined. Dibromostyrene was moderately to highly irritating (WIL Research 1983 and 1987) to the skin of rabbits and slightly irritating (WIL Research, 1987) to the eyes of rabbits.

4.5.2 Sensitization

Dibromostyrene was not a sensitizer in guinea pigs (WIL Research 1987).

4.5.3 Summary/Test plan for mammalian toxicity

Adequate acute and repeated dose oral toxicity studies show ingestion of fairly large amounts of dibromostyrene is required to produce toxicity. The material is also not irritating to the skin or eyes, and is not sensitizing to humans.

Adequate studies show that dibromostyrene is not a mutagen and does not possess the potential to produce chromosomal aberrations. Developmental studies in the rat and rabbit have adequately characterized the teratogenic potential of dibromostyrene. A two-generation reproduction toxicity study in rats has also provided adequate information on the reproductive effects that may be expected when dibomostyrene is administered orally in fairly large doses.

5. Summary

In summary, valid data are present to satisfy all physical/chemistry and environmental fate toxicity endpoints. No ecotoxicity data are available on aquatic vertebrates, invertebrates, or plants. This testing is necessary and will be performed as indicated in the test plan.

Existing studies on acute, repeated dose, genetic (mutations and chromosomal aberrations), reproductive and developmental toxicity are sufficient to satisfy these endpoints. Data for eye and skin irritation and sensitization are adequate (although not required).

6. References

See IUCLID reference set.

201-14931

IUCLID

Data Set

Existing Chemical	:	ID: 125904-11-2
CAS No.	:	125904-11-2
Chemical characterisation	:	Dibromostyrene
Product name	:	DBS, CN-19
Synonym	:	DBS; Dibromostyrene; CN-19; Step III; Benzene, ethenyl, aryl brominated derivatives; Brominated styrene

Producer Related Part

Company	:	GREAT LAKES CHEMICAL CORPORATION
Creation date	:	05.06.2002

Substance Related Part

Company	:	GREAT LAKES CHEMICAL CORPORATION
Creation date	:	05.06.2002
Memo	:	
Printing date	:	11.12.2003
Revision date	:	
Date of last Update	:	11.12.2003
Number of Pages	:	26
Chapter (profile)	:	Chapter: 1.0.1, 1.2, 1.6.1, 1.6.2, 1.8, 1.9, 1.14.1, 1.14.2, 1.14.3, 1.15, 2, 3, 4, 5, 7
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

1.2 SYNONYMS

Benzene, ethenyl, aryl brominated derivatives
26.06.2003

Brominated styrene
26.06.2003

CN-19
26.06.2003

DBS
26.06.2003

Dibromostyrene
26.06.2003

Step III
26.06.2003

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

2.1 MELTING POINT

Value	:	= -37 °C
Sublimation	:	
Method	:	other: Estimated
Year	:	
GLP	:	no data
Test substance	:	
Reliability	:	(4) not assignable

11.12.2003 (4)

2.2 BOILING POINT

Value	:	= 95 °C at
Decomposition	:	
Method	:	other: Experimental
Year	:	
GLP	:	no data
Test substance	:	
Reliability	:	(4) not assignable

11.12.2003 (4)

2.3 DENSITY

Type	:	relative density
Value	:	= 1.83 at ° C
Method	:	other: Experimental
Year	:	
GLP	:	no data
Test substance	:	
Reliability	:	(4) not assignable

11.12.2003 (4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .09999 hPa at 30° C
Decomposition	:	
Method		other (measured)
Year	:	
GLP	:	no data
Test substance	:	
Reliability	:	(4) not assignable

11.12.2003 (4)

2.5 PARTITION COEFFICIENT

Method		OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	
GLP	:	yes
Test substance	:	other TS: DBS, Batch 603217M1, purity=99.52% (10% mono, 85% di and 5% tri)
Method	:	The n-octanol/water partition coefficient was determined by performing the flask-shaking method. The method consisted of shaking the solute (DBS) weth twe immiscible solvents (n-octanol and water) over a period of time and analyzing both phases for the solute concentration using an analytical method developed at the testing facility. An initial feasibility trial was performed to establish whether or not a shake flask experimental design was appropriate for the test substance. The criteria for method rejection were if the test substance was miscible or infinitly soluble in both water and n-octanol and/or an inseparable emulsion was formed. The definitive portion of the test was conducted with presaturated solvents at three n-octanol/water solvent ratios (1:5, 1:10, and 1:20).
Remark	:	Also ran per U.S. EPA Product Properties Test Guidelines OPPTS 830.7550. Sponsor: Great Lakes Chemical Corp.
Result	:	The n-octanol/water partition coefficient log Kow values for monobromostyrene, dibromostyrene and tribromostyene were calculated as 3.94 +/- 0.0678 (CV=1.72%), 4.43 +/- 0.0567 (CV=1.28%), and 4.53 +/- 0.0836 (CV=1.85%), respectively. Procedurally corrected recoveries for monobromostyrene, dibromostyrene and tribromostyrene were calulated to be 103 +/- 3.19%, 107 +/- 4.64% and 109 +/- 6.11%, respectively.
Conclusion	:	The n-octanol/water partition coefficient log Kow values for monobromostyrene, dibromostyrene and tribromostyene were calculated as 3.94 +/- 0.0678 (CV=1.72%), 4.43 +/- 0.0567 (CV=1.28%), and 4.53 +/- 0.0836 (CV=1.85%), respectively.
Reliability	:	(1) valid without restriction

09.12.2003 (28)

2.6.1 WATER SOLUBILITY

Method	:	OECD Guide-line 105 "Water Solubility"
Year	:	
GLP	:	yes
Test substance	:	other TS: DBS, Batch 603217M1, purity=99.52% (10% mono, 85% di and 5% tri)
Method	:	The water solublity of DBS was determined at a temperature of 20 +/- 0.5 degrees C. The test consisted of equilibration of an excess amount of test substance with HPLC-grade bottled reagent water at elevated temperature (30 degrees C) for 24 and 48 hours (and 72 hours, if required) followed by equilibration at 20 degrees C for 24 hours prior to analysis and quantitation of soluble test substance in the aqueous phase.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Duplicate sub-samples were removed from the appropriate bottles after 24 and 48 hours of shaking in a water bath maintained at 30 +/- 1.0 degrees C and following 24 hours of equilibration at 20 +/- 0.5 degrees C. Analysis of these aqueous sub-samples yielded water solubility concentrations for DBS that were dependent on the component of the DBS test substance being monitored. Mean measured DBS concentrations for the 24 and 48-hour samples were well within the 15% criterion of the protocol. Consequently, analysis of the 72-hour sample was not required. The mean water solubility (n=4) for DBS at 20 degrees C was 6.91 +/- 0.0871, 49.2 +/- 1.45 and 1.03 +/- 0.104 mg/L using the dibromo-,

monobromo-, and tribromostyrene surrogates for the test substance, respectively, to quantitate DBS concentrations.

Conclusion : The mean water solubility (n=4) for DBS at 20 degrees C was 6.91 +/- 0.0871, 49.2 +/- 1.45 and 1.03 +/- 0.104 mg/L using the dibromo-, monobromo-, and tribromostyrene surrogates for the test substance, respectively, to quantitate DBS concentrations.

Reliability : (1) valid without restriction

09.12.2003 (27)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

Memo : Determination of Dissociation Constant of Dibromostyrene (DBS)

Method : The tritration method was used to determine the dissociation constant K (expressed as its log value, pK) of DBS in HPLC-grade bottled reagent water.

Remark : Sponsor: Great Lakes Chemical Corp.

Result : pKa values determined for reference standards (phosphoric acid and 4-nitrophenol) were in good agreement with literature values. The pKa estimate obtained for DBS in the preliminary trial was 5.41. The preliminary results also indicated that a relatively weak NaOH solution would be required. Therefore, a 0.001 N NaOH solution was prepared and stanardized for use in the definitive trial.

The pKa value of DBS was determined to be 6.72 (SD=0.0855, CV=1.27%) at 20 degrees C.

Conclusion : The pKa value of DBS was determined to be 6.72 (SD=0.0855, CV=1.27%) at 20 degrees C.

Reliability : (1) valid without restriction

09.12.2003 (3)

3.1.1 PHOTODEGRADATION

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	at degree C
t1/2 pH9	:	at degree C
Deg. Product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	
GLP	:	yes
Test substance	:	other TS: DBS, Batch 603217M1, purity = 99.52% (10% mono, 85% di and 5 % tri)
Method	:	Hydrolysis of DBS in aqueous buffered media (pH 4, 7, and 9) was investigated at a concentration of 1.00 mg/L. The selected concentration was less than one-half of the water solubility of the dominate (85%) dibromostyrene constiuent of the test substance (6.91 +/- 0.0871 mg DBS/L). A preliminary test was conducted with fortified samples in pH 4, 7 and 9 buffer solutions over a five-day period at 50 +/- 1 degrees C. The definitive test was conducted with fortified samples in pH 4, 7 and 9 buffer solutions maintained at 15 and 25 degrees C. Samples were subjected to seven sampling intervals over a 30-day period. Samples incubated at 15 degrees C were collected on Day 0. Thereafter samples were collected on Days 2, 3, 10, 25 and 30. Samples incubated at 25 degrees C were collected at Days 0, 2, 3, 10, 17 and 30. Duplicate samples were analyzed at each interval for the 25 degree test, while single samples were analyzed from the 15 degrees C test. Each of the constituents of DBS (mono-, di- and tribromostyrene) were analyzed to determine the test substance concentration in the samples.
Remark	:	Sponsor: Great Lakes Chemical Corp. Study also compliant U.S. EPA Product Properties Test Guidlines, OPPTS 835.2110, Hydrolysis as a Function of pH.
Result	:	DBS was determined to be hydrolytically stable at 15 degrees C when monitoring DBS with the monobromostyrene constituent at pH 4 and 9. Based on the dibromostyrene constituent, DBS was determined to be hydrolytically stable at pH 4 and 7, but was marginally hydrolytically unstable at pH 9 (t1/2 = 177 days). Based on the tribromostyrene constituent, DBS was determined to be hydrolytically stable at PH 7, but was unstable at Ph 4 (t1/2 = 46 days) and pH 9 (t1/2 = 149 days). At 25 degrees C, DBS degraded at all pH levels. Half-lives based on monobromo-, dibromo-, and tribromostyrene ranged from 39 - 43, 50 - 59 and 37 - 49 days respectively. Half-lives based on pH ranged from 37 - 50 (pH 4), 39 - 59 (pH 7) and 40 - 52 (pH 9) days.
Conclusion	:	Half-lives based on monobromo-, dibromo-, and tribromostyrene ranged from 39 - 43, 50 - 59 and 37 - 49 days respectively. Half-lives based on pH ranged from 37 - 50 (pH 4), 39 - 59 (pH 7) and 40 - 52 (pH 9) days.
Reliability	:	(1) valid without restriction

09.12.2003 (2)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	adsorption
Media	:	
Air (level I)	:	
Water (level I)	:	
Soil (level I)	:	
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other: OECD Guidline 121
Year	:	2001
Method	:	The DBS test substance and a series of reference substances bracketing the applicable log Koc range of the HPLC estimation method were separately prepared in methanol and diluted in a 55% acetonitrile:45% HPLC grade reagent water (v/v) HPLC mobile phase. The reference and DBS solutions were sequentially injected into an HPLC system operating under standardized isocratic, reverse-phase operating conditions employing a cynopropyl-based stationary phase. Capacity factors were calculated for the reference standards and DBS using thiourea to estimate column dead time (i.e. the retention time of a known unretained reference standard). The logarithms of the capacity factors were then plotted against published log Koc values to establish a linear regression calibration. The capacity factors of DBS were used in conjuction with the linear regression equations to calculate the log Koc range for DBS.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Reference standards were injected at the beginning and at the end of the HPLC sequence. The capacity factors of each standard were calculated based upon their retention times. The monobromostyrene, dibromostyrene and tribromostyrene eluted at times of 5.435, 7.067 and 9.275 minutes, respectively. The retention times for all three peaks were bracketed by the reference standards. Mean log Koc values were calculated for monobromostyrene, dibromostyrene and tribromostyrene as 3.27 +/- 0.000274, 3.79 +/- 0.000551 and 4.26 +/- 0.000762, respectively.
Test substance	:	DBS, Batch 603217M1, purity = 99.52% (10% mono, 85% di and 5 % tri)
Conclusion	:	The mean log Koc values for monobromostyrene, dibromostyrene and tribromostyrene were calculated as 3.27 +/- 0.000274, 3.79 +/- 0.000551 and 4.26 +/- 0.000762, respectively. Based on these data, the test substance is expected to adsorb to soil and not partition to other compartments.
Reliability	:	(1) valid without restriction

11.12.2003 (1)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: corn oil
Value	:	> 200 mg/kg bw
Method	:	other: Title 49 (DOT), 173.343
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene CN-20-0019.
Method	:	A DOT Class B poison assay of Dibromostyrene was performed in rats. Five male and 5 female fasted rats were administered the test material in corn oil as a single gavage dose of 0.050 g/kg.
Remark	:	Sponsor: Velsicol Chemical Corp.
Result	:	There was no mortality in the study. Dibromostyrene is not considered a class B poison (DOT classification).
Reliability	:	(1) valid without restriction

11.12.2003 (12)

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	30
Vehicle	:	
Value	:	= 6327 mg/kg bw
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene (899 00 00) 31874H, Ref. 10-27-82.
Method	:	The oral toxicity of Dibromostyrene to rats was determined. In a preliminary study, 5 male and 5 female rats were administered a single gavage dose of test material at 5.0 g/kg. One of ten animals died and signs of systemic toxicity were observed in all 10. In this study 3 groups (5 males, 5 females) were administered a single gavage dose at 2.750. 3.440 or 4.125 ml/kg, calculated as 5.00, 6.25 or 7.50 g/kg (1 ml approximately 1.83g). Animals were observed for toxicity and mortality for 14 days following dosing.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Mortality was:

Dose (g/kg)	Animals Dead/Total Males	Females
5.00	0/5	0/5
6.25	3/5	2/5
7.50	5/5	3/5

Clinical signs of toxicity on the day of dosing included ataxia, lethargy, prostration, salivation, lacrimation, and urine stains. Positive gross pathologic findings for animals dying on test included stomach distended with food, forestomach with shaggy white or chalky white material, hindstomach reddened or pale with or without focal hemorrhage, and intestines reddened.

The LD50 (95% C.I.) of Dibromostyrene administered orally to rats was:
Males: 5.790 (4.826 - 6.946) g/kg
Females: 6.937 (5.906 - 8.148 g/kg
Combined: 6.327 (5.622 - 7.121) g/kg

Reliability	:	(1) valid without restriction

11.12.2003 (13)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: DOT Class B poison
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male
Number of animals	:	10
Vehicle	:	
Exposure time	:	1 hour(s)
Value	:	> 3.1 mg/l
Method	:	other: CFR 49, part 173.343 (2) (DOT)
Year	:	1976
GLP	:	yes
Test substance	:	other TS: Dibromostyrene (CN-20-0019)
Method	:	A DOT Class B poison test for inhalation toxicity of Dibromostyrene was performed in male rats. Male rats were exposed to a nominal concentration of 2 mg/l for 1 hour. They were exposed in two groups of 5 rats each to nominal concentrations of 3.1 and 2.8 mg/l of air. Animals were oserved for 2 days following exposures.
Remark	:	Sponsor: Velsicol Chemical Corp.
Result	:	There were no mortalities in the study. Dibromostyrene is not considered a Class B poison by the inhalation route.
Reliability	:	(1) valid without restriction

11.12.2003 (12)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Value	:	> 2000 mg/kg bw
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene (899 00 00) 31874H, ref. 10-27-82.
Method	:	Acute dermal toxicity of Dibromostyrene was evaluated in rabbits. The test material at a dose of 2000 mg/kg body weight was applied to clipped, abraded sites on the backs of 5 male and 5 female rabbits. Each test site was occluded with a layer of 4-ply gauze and the trunk of the rabbit wrapped with rubber latex dental dam which was taped at the edges for form an airtight occlusive wrap. Twenty-four hours later the bandages and residual material were removed and the site s wiped with a paper towel.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	There was no mortality; therefore, an LD50 could not be calculated. The LD50 of Dibromostyrene is greater than 2.0 g/kg body weight.
Reliability	:	(1) valid without restriction

11.12.2003 (14)

Type	:	other: DOT Class B poison
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	

Value	:	> 200 mg/kg bw
Method	:	other: Title 49 (DOT), 173.343.
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene CN-20-0019.
Method	:	A DOT Class B poison assay was performed with Dibromostyrene in rabbits. A single dose of 0.2 g/kg of Dibromostyrene was applied directly to a site on the clipped back of each of 5 male and 5 female rabbits. the sites were covered with a gauze bandage and overwrapped with Saran Wrap and Elastoplast tape. Collars were applied during exposure. Twenty-four hours later the bandages were removed and the backs wiped clean.
Remark	:	Sponsor: Velsicol Chemical Corp.
Result	:	There were no mortalities during the 2 day observation period. Dibromostyrene is not considered a Class B poison by the dermal route of administration.
Reliability	:	(1) valid without restriction

11.12.2003 (12)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
PDII	:	6.6
Result	:	highly irritating
EC classification	:	irritating
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene.
Method	:	Primary dermal irritation potential of Dibromostyrene was evaluated in rabbits. 0.5 ml of test material was applied to each of 4 sites (2 intact and 2 abraded) on the clipped backs of 3 male and 3 female rabbits. Each test site was occluded with a gauze patch, secured with micropore tape. The trunk of each rabbit was wrapped with rubber latex dental dam and overwrapped with Elastoplast tape. Twenty-four hours later the bandages and residual material were removed and the sites wiped with a paper towel.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	The primary dermal irritation index of 6.6 classifies Dibromostyrene as severely irritating.
Reliability	:	(1) valid without restriction

11.12.2003 (16)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6
PDII	:	4.1
Result	:	moderately irritating
EC classification	:	irritating
Method	:	EPA OPP 81-5
Year	:	
GLP	:	yes

Test substance	:	other TS: Dibromostyrene, Sample #1375-20-3.
Method	:	Primary dermal irritation potential of Dibromostyrene was evaluated in rabbits. 0.5 ml of test material was applied to one intact site on the clipped back of each of 3 male and 3 female rabbits. Each test site was covered with a gauze patch that was overwrapped with a gauze binder, secured with Dermiform tape (semi-occluded). Plastic restraint collars were applied. Four hours later the bandages and residual material were removed and the sites wiped with a paper towel.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	There were no deaths or remarkable body weight changes. The Primary Irritation Index was calculated to be 4.1. Dibromostyrene received a descriptive rating classification of moderately irritating.
Reliability	:	(1) valid without restriction

11.12.2003 (20)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
PDII	:	
Result	:	
EC classification	:	
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene CN-20-0019.
Method	:	A DOT dermal corrosivity test of Dibromostyrene was performed in rabbits. 0.5 ml of test material was applied to a site on the clipped backs of 3 male and 3 female rabbits. Each test site was occluded with a gauze patch, secured with micropore tape overwrapped with Saran Wrap and secured with Elastoplast tape. The rabbits were collared during exposure. Four hours later the bandages and residual material were removed and the sites wiped with a wet paper towel.
Remark	:	Sponsor: Velsicol Chemical Corp.
Result	:	Primary dermal irritation scores were: 4 hrs 3.1 24 hrs 3.5 48 hrs 3.3 In accordance with Title 49, 173.1200, Appendix A, this compound is not considered to be corrosive.
Reliability	:	(1) valid without restriction

11.12.2003 (12)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	.5 minute(s)
Comment	:	rinsed after (see exposure time)
Number of animals	:	9
Result	:	slightly irritating
EC classification	:	irritating
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene (899 00 00) 31874H, ref. 10-27-82.

Method	:	Primary eye irritation potential of Dibromostyrene was evaluated in rabbits. 0.1 ml of undiluted test material was instilled into the conjunctival sac of the right eye of 9 albino rabbits. The lids were held closed for 1 sec and released. Approximately 20 to 30 seconds after instillation, the treated eyes of three of the rabbits were held open and rinsed for 1 minute with distilled water.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	No signs o f systemic toxicity or mortality occurred. Positive scores involved only the conjunctiva. Mean scores were similar in the rinsed and not rinsed groups. The primary irritation index was 11.00 with a mean score of greater than 0 at 72 hours. This classifies Dibromostyrene as mildly irritating. The score was only slightly decreased for the rinsed group.
Reliability	:	(1) valid without restriction

11.12.2003 (15)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	
Comment	:	not rinsed
Number of animals	:	6
Result	:	slightly irritating
EC classification	:	irritating
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, sample #1375-20-3.
Method	:	Primary eye irritation potential of Dibromostyrene was evaluated in rabbits. 0.1 ml of undiluted test material was instilled into the conjunctival sac of the right eye of 6 albino rabbits. The lids were held closed for 1 sec and released.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	The Maximum Average Score was 7.3 at 1 hour. This classifies Dibromostyrene as mildly irritating.
Reliability	:	(1) valid without restriction

11.12.2003 (21)

5.3 SENSITIZATION

Type	:	no data
Species	:	guinea pig
Concentration	:	Induction 25 % occlusive epicutaneous Challenge 5 % occlusive epicutaneous
Number of animals	:	8
Vehicle	:	other: acetone
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, #1375-20-3.
Method	:	Dibromostyrene was tested in guinea pigs for dermal sensitization. The test material, 25% w:v in acetone was applied to the shaved intact dorsal skin of 6 male and 6 female guinea pigs a total of 9 times during the induction phase. 0.4 ml doses were applied three times/week for 3 weeks under 25 mm Hilltop Chambers that were occluded with latex dental dam and secured with Elastoplast Tape. After 6 hours exposure, bandages and chambers were removed and residual material removed with paper towels

moistened with water. Following a period of 2 weeks, a 5% concentration was administered to previously unexposed sites (0.4 ml) as a challenge (same procedure as induction). The sites were scored.

Remark : Sponsor: Great Lakes Chemical Corp.

Result : Challenge dose findings in the test group were limited to very slight reactions that were observed for 5 animals. Dibromostyrene is not a sensitizing agent in the albino guinea pig.

Reliability : (1) valid without restriction

11.12.2003 (17)

5.4 REPEATED DOSE TOXICITY

Species : rat

Sex : male/female

Strain : other: Crl:CD(R) BR

Route of admin. : gavage

Exposure period : 28 day

Frequency of treatment : daily

Post obs. period :

Doses : 200, 400, 800 and 1600 mg/kg bw

Control group : yes, concurrent vehicle

Method :

Year :

GLP : yes

Test substance : other TS: Dibromostyrene, 1371-094-01.

Method : Potential adverse effects of Dibromostyrene were evaluated in a 28-day range-finding study in rats. Dibromostyrene admixed in corn oil was administered by gavage to four groups of 5 male and 5 female rats at doses of 200, 400, 800 and 1600 mg/kg/day for 21 days. A concurrent control group (5 males, 5 females) received corn oil on a comparable regimen. Dose levels were then increased from 200, 400 and 800 mg/kg to 2400, 3600 and 5400 mg/kg, respectively, for dosing to necropsy. The vehicle control and 1600 mg/kg groups remained the same.

Remark : Sponsor: Great Lakes Chemical Corp.

Result : All animals dosed at 1600 mg/kg survived to the scheduled necropsy. Evidence of systemic toxicity included clinical findings, male mean body weight data, mean absolute and relative liver weights and microscopic hepatic changes.

Up to and including day 21 the only treatment related effects noted in the 400 and 800 mg/kg groups were clinical signs of toxicity (salivation, staining and matting around the mouth, etc). There was no evidence of toxicity in the 200 mg/kg group.

Nine of ten animals dosed at 200 mg/kg for 21 days and increased to 2400 mg/kg died within 3 days of the initial higher dose. The surviving female was dosed with 2400 mg/kg for 9 days prior to sacrifice. Clinical observations of severe toxicity were observed at the higher dose level.

All animals dosed at 400 mg/kg for 21 days and increased to 3600 mg/kg died within three days of the initial higher dose.

All animals dosed at 800 mg/kg for 21 days and increased to 5400 mg/kg died within three days of the initial higher dose.

[A NOAEL is stated in the report (200 mg/kg/day); however, as this dose was not administered for 28 days and only one of these animals was necropsied (following 9 daily doses at a much higher dose), it does not appear to be a valid NOAEL.]

Reliability : (2) valid with restrictions

11.12.2003 (22)

Species : rat

Sex : male/female

Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	28 days
Frequency of treatment	:	daily
Post obs. period	:	
Doses	:	1, 10, 50 and 100 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 100 mg/kg bw
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, Sample #1375-20-2 and -3.
Method	:	Potential adverse effects of Dibromostyrene were evaluated in a 28-day range-finding study in rats. Dibromostyrene admixed in corn oil was administered by gavage to four groups of 5 male and 5 female rats at doses of 1, 10, 50 and 100 mg/kg/day for 28 days. A concurrent control group (5 males, 5 females) received corn oil on a comparable regimen.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Survival was 100%. There were no effects that could be attributed to treatment observed in the study. The NOAEL for systemic toxicity of Dibromostyrene is 100 mg/kg/day.
Reliability	:	(1) valid without restriction

11.12.2003 (18)

Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD(R)BR
Route of admin.	:	gavage
Exposure period	:	90 days
Frequency of treatment	:	daily
Post obs. period	:	30 days
Doses	:	130, 300, 700 and 1600 mg/kg bw
Control group	:	yes, concurrent vehicle
NOAEL	:	= 130 mg/kg bw
LOAEL	:	= 300 mg/kg bw
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, 1371-094-02 through 1371-94-08 and -012 through -15.
Method	:	Potential adverse effects of Dibromostyrene were evaluated in a 90-day subchronic toxicity study in rats with a 4-week recovery period. Dibromostyrene suspended in corn oil was administered by gavage to four groups of 20 male and 20 female rats (F0) at doses of 130, 300, 700 and 1600 mg/kg/day. A concurrent control group (20 males, 20 females) received corn oil on a comparable regimen. Following 90 days of dosing, 5 animals/sex/group remained on study for a 30 day recovery period.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	The only treatment related clinical finding was salivation or evidence of salivation noted at 1 hour post dosing. An adverse body weight effect was apparent in males at 1600 mg/kg throughout treatment; mean body weight gain was decreased during the first week of dosing and sporadically throughout dosing. Mean food consumption values were consistently increased in males and females at 1600 mg/kg throughout treatment and males at 700 mg/kg. Mean hematocrit and MVC were increased and hemoglobin, MCH and MCHC were decreased at 1600 mg/kg at the 30 day evaluation. MCH was increased and hemoglobin and MCHC were decreased at 1600 mg/kg at the 90 day evaluation. These trends in MCV, hemoglobin and MCHC were

also observed at 300 and 700 mg/kg at the 30 or 90 day evaluations, although the differences from control were not necessarily dose related or consistent between males and females. Hypoglycemic trends were apparent at 300, 700 and 1600 mg/kg at 30 and 90 days.

Serum bromide and tissue bromine concentrations were increased and generally dose related in all groups at 90 days. Serum bromide and tissue bromine levels in treated groups decreased to near control values at the end of the recovery.

Urine volume was increased in males at 300 and 700 mg/kg and in males and females at 1600 mg/kg at 30 days. Mean urine volumes remained increased in males at 700 mg/kg and males and females at 1600 mg/kg at 90 days.

Dose related increases in absolute and relative liver weights were apparent in females at 700 and 1600 mg/kg at 90 days. Liver weight relative to final body weight was increased in females at 300 mg/kg although absolute liver weight was comparable to control. Relative kidneys and testes weights were increased in males at 1600 mg/kg; however, mean final body weight was decreased in this group. Female liver weights in the 1600 mg/kg remained increased at the recovery sacrifice.

Treatment related microscopic changes were observed in the liver, kidneys and possibly urinary bladder of animals at 1600 mg/kg and in the liver of animals at 700 mg/kg at 90 days. These effects consisted of minimal to mild hypertrophy of the centrilobular parenchymal cells in the liver (indicative of enzyme induction), areas of nephrosis (a noninflammatory lesion) in the kidneys and an increased incidence of minimal hyperplasia of the urinary bladder epithelium.

Reliability : (1) valid without restriction
11.12.2003 (19)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Chromosomal aberration test
System of testing	:	Chinese hamster ovary (CHO) cells
Concentration	:	0.005 to 0.04 ul/ml
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	ambiguous
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, lot #1375-45-1.
Method	:	Dibromostyrene was tested in the chromosome aberration assay using Chinese hamster ovary cells. Cells were treated at 0.04, 0.02, 0.01 and 0.005 ul/ml in the absence of a metabolizing enzyme fraction and at 0.03, 0.02, 0.01 and 0.005 ul/ml in the presence of activation.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	A statistically significant increase in chromosome aberrations was observed at 0.01 and 0.005 ul/ml in the nonactivated study and at 0.03 ul/ml in the activated study. Dibromostyrene was considered a suspect positive in the CHO chromosome aberration assay.
Reliability	:	(1) valid without restriction

11.12.2003 (7)

Type	:	Chromosomal aberration test
System of testing	:	Chinese hamster ovary (CHO) cells
Concentration	:	1, 5 and 15 ug/ml (-S-9); 5, 25 and 75 (+S-9)
Cycotoxic conc.	:	25 ug/ml (-S-9); 100 ug/ml (+S-9)
Metabolic activation	:	with and without
Result	:	negative
Method	:	

Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, 1371-083-1.
Method	:	Dibromostyrene was evaluated for potential to induce chromosome aberrations in CHO cells in culture in the absence and presence of a metabolizing enzyme fraction. Dose levels were based on results of a preliminary cytotoxicity assay. In the absence of S-9 doses were 1, 5 and 15 ug/ml and in the presence of S-9 doses were 5, 25 and 75 ug/ml. Concurrent solvent and positive controls were run.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Results of the assay indicate no significant increases in aberrations/cell or proportion of aberrant metaphases at any dose evaluated with or without S-9. Dibromostyrene is negative in its ability to induce chromosome aberrations (clastogenicity) under the experimental conditions of this assay.
Reliability	:	(1) valid without restriction

11.12.2003 (9)

Type	:	Chromosomal aberration test
System of testing	:	Chinese hamster ovary (CHO) cells
Concentration	:	2.5, 10 and 35 ug/ml (-S-9); 9, 50 and 90 ug/ml (+S-9)
Cycotoxic conc.	:	50 ug/ml (-S-9); 250 ug/ml (+S-9)
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, #1371-083-2.
Method	:	Dibromostyrene was evaluated for potential to induce chromosome aberrations in CHO cells in culture in the absence and presence of a metabolizing enzyme fraction. Dose levels were based on results of a preliminary cytotoxicity assay. In the absence of S-9 doses were 2.5, 10 and 35 ug/ml and in the presence of S-9 doses were 9, 50 and 90 ug/ml. Concurrent solvent and positive controls were run.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Results of the assay indicate no significant increases in aberrations/cell or proportion of aberrant metaphases at any dose evaluated with or without S-9. However, the high dose (90 ug/ml) with S-9 resulted in a statistically significant increase in aberrations/cell. Dibromostyrene is negative in its ability to induce chromosome aberrations (clastogenicity) under the experimental conditions of this assay.
Reliability	:	(1) valid without restriction

11.12.2003 (10)

Type	:	Chromosomal aberration test
System of testing	:	Chinese hamster ovary (CHO) cells
Concentration	:	2.5, 10 and 35 ug/ml (-S-9); 5, 25 and 75 ug/ml (+S-9)
Cycotoxic conc.	:	50 ug/ml (-S-9); 100 ug/ml (+S-9)
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, #1371-083-2.
Method	:	Dibromostyrene was evaluated for potential to induce chromosome aberrations in CHO cells in culture in the absence and presence of a metabolizing enzyme fraction. Dose levels were based on results of a preliminary cytotoxicity assay. In the absence of S-9 doses were 2.5, 10 and 35 ug/ml and in the presence of S-9 doses were 5, 25 and 75 ug/ml. Concurrent solvent and positive controls were run.
Remark	:	Sponsor: Great Lakes Chemical Corp.
Result	:	Results of the assay indicate no significant increases in aberrations/cell or proportion of aberrant metaphases at any dose evaluated with or without S-

9. Dibromostyrene is negative in its ability to induce chromosome aberrations (clastogenicity) under the experimental conditions of this assay.

Reliability : (1) valid without restriction
11.12.2003 (11)

Type : Ames test
System of testing : Salmonella plate incorporation
Concentration : 0.001, 0.005, 0.010, 0.050, 0.10, 0.25 and 0.50 ul/plate
Cycotoxic conc. : 150 ul/plate
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP : yes
Test substance : other TS: Dibromostyrene, #721-187.
Method : Dibromostyrene was tested for mutagenic activity in Salmonella typhimurium (5 strains) in the absence and presence of metabolic activation. Concentrations tested ranged from 0.001 to 0.50 ul/plate.
Remark : Sponsor: Great Lakes Chemical Corp.
Result : The test material did not exhibit genetic activity in any of the assays conducted and was considered not mutagenic.
Reliability : (1) valid without restriction
11.12.2003 (5)

Type : Mammalian cell gene mutation assay
System of testing : CHO/HGPRT
Concentration : 5, 10, 15, 20 and 25 nl/ml (-S-9); 25, 40, 55, 60 and 70 nl/ml (+S-9)
Cycotoxic conc. : survival <50% at 25 nl/ml (-S-9) and 55 nl/ml (+S-9)
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP : yes
Test substance : other TS: Dibromostyrene.
Method : Dibromostyrene was tested in the CHO/HGPRT mutation assay in the absence and presence of an Aroclor-induced rat liver S-9 activation system. The assay was conducted at dose levels of 25, 20, 15, 10 and 5 nl/ml in the non-activated study and at 70, 60, 55, 40 and 25 ul/ml in the presence of S-9.
Remark : Sponsor: Great Lakes Chemical Corp.
Result : Dibromostyrene was negative in the CHO/HGPRT mutation assay.
Reliability : (1) valid without restriction
11.12.2003 (6)

Type : Unscheduled DNA synthesis
System of testing : Rat primary hepatocytes
Concentration : 8 doses ranging from 0.001 to 0.03 ul/ml
Cycotoxic conc. : 0.1 to 10 ul/ml
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP : yes
Test substance : other TS: Dibromostyrene, lot #1375-45-1.
Method : Dibromostyrene was tested in the unscheduled DNA synthesis test using rat primary hepatocytes. The test article was tested at eight dose levels ranging from 0.0001 ul/ml to 0.1 ul/ml and was fully evaluated at five dose levels from 0.001 ul/ml to 0.03 ul/ml.
Remark : Sponsor: Great Lakes Chemical Corp.
Result : The test article did not cause a significant increase in the mean number of net nuclear grain counts at any dose level. It is considered negative in this study.

Reliability	:	(1) valid without restriction
11.12.2003		(8)

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	70 days prior to mating (F0) through lactation day 21 for F2 generation
Frequency of treatment	:	daily
Premating exposure period		
Male	:	70 days
Female	:	70 days
Duration of test	:	through lactation day 21 of F2 generation
Doses	:	100, 400 and 1600 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL Parental	:	= 100 mg/kg bw
NOAEL F1 Offspr.	:	< 100 mg/kg bw
NOAEL F2 Offspr.	:	= 400 mg/kg bw
Method	:	OECD Guide-line 416 "Two-generation Reproduction Toxicity Study"
Year	:	1983
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, 1770-014-06 through 1770-014-17 and 1770-018-033.
Method	:	Potential adverse effects of Dibromostyrene on the reproductive capabilities of the F0 and F1 generations and neonatal viability and growth were evaluated. Dibromostyrene in corn oil was administered by gavage to three groups of 35 male and 35 female rats (F0) at doses of 100, 400 and 1600 mg/kg/day. A concurrent control group (35 males, 35 females) received corn oil on a comparable regimen. F0 animals were treated for at least 70 days prior to the first pairing and throughout subsequent phases of the study until 1 day prior to necropsy (following weaning of pups). Offspring from the F0 animals were selected to constitute the F1 generation (35/sex/group). Unselected pups were necropsied following weaning. Selected pups were treated from day 22 post partum, for at least 70 days prior to the first pairing and throughout subsequent phases of the study until 1 day prior to necropsy (following weaning of pups). Offspring from the F1 animals (F2 pups) were necropsied following weaning.
Remark	:	Sponsor: Great Lakes Chemical Corp. Study also compliant EPA TSCA Guidelines, 40 CFR Part 798.4700, 1987.
Result	:	Survival was affected at 1600 mg/kg. Body weight gains and/or food consumption were inhibited for males at 400 mg/kg and for males and females at 1600 mg/kg. Dark red or reddened adrenal glands and hemorrhagic thymus glands were the primary necropsy findings for 1600 mg/kg F0 animals that died. Mean absolute testes weight was significantly reduced in F1 males at 1600 mg/kg. Increased liver weights were apparent in the F0 and F1 animals at

400 and 1600 mg/kg. Increased weights and treatment-related microscopic lesions were observed in the kidney of F0 and F1 animals at 1600 mg/kg; the microscopic lesions consisted of tubular dilatation, nephrosis and/or papillary necrosis. Increased kidney weights, but no microscopic lesions, were noted in F0 and F1 males at 400 mg/kg.
In the F1 and F2 neonates, adverse effects were noted at 400 and 1600 mg/kg. Live litter sizes were slightly decreased (non-significant) in F1 pups at 400 mg/kg and in F1 and F2 pups at 1600 mg/kg. Changes in the clinical condition of the pups (body cool to the touch) were observed in both generations at both dose levels. Neonatal body weights were reduced at 400 mg/kg beginning days 28 (F1) or 21 (F2) postpartum and at 1600 mg/kg beginning on day 1 (F1 and F2).
At 100 mg/kg, the only effect was an increase in kidney and liver weights in F1 males.

Conclusion : A potential adverse effect on fertility was observed in F1 males at 1600 mg/kg. No other adverse effects on reproductive parameters were observed in the F0 and F1 generations at any dose. Neonatal toxicity in F1 and F2 generations at 400 and 1600 mg/kg was exhibited by slightly decreased live litter sizes, decreased pup viability, changes in the clinical condition of the pups and decreased pup body weights. F1 and F2 neonates at 100 mg/kg were unaffected by parental treatment.
The NOAEL for reproductive toxicity was 400 mg/kg/day; 100 mg/kg/day was the NOAEL for neonatal toxicity. The NOAEL for parental toxicity was 100 mg/kg/day in the F0 generation and <100 mg/kg/day in the F1 generation.

Reliability : (1) valid without restriction
11.12.2003 (23)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rabbit
Sex	:	female
Strain	:	New Zealand white
Route of admin.	:	gavage
Exposure period	:	Gestation Day 7 through 19
Frequency of treatment	:	daily
Duration of test	:	Gestation Day 29
Doses	:	50, 250, 500 and 700 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL Maternalt.	:	= 250 mg/kg bw
NOAEL Teratogen	:	= 500 mg/kg bw
Method	:	EPA OTS 798.4900
Year	:	1987
GLP	:	yes
Test substance	:	other TS: Dibromostyrene 1770-014-06 and -07.

Method : The potential maternal and developmental toxicity of Dibromostyrene were evaluated in rabbits (range-finding). Dibromostyrene in corn oil was administered by gavage to four groups of 6 inseminated rabbits as a single daily dose of 50, 250, 500 and 700 mg/kg from days 6 through 19 of gestation. Six control females were dosed concurrently with corn oil on a comparable regimen. All surviving females were sacrificed for a Cesarean section on day 29 of gestation.

Remark : Sponsor: Great Lakes Chemical Corp.

Result : Four and 3 deaths occurred at 700 and 500 mg/kg, respectively, and 2 animals at 700 and 1 at 500 were sacrificed. Significant mean body weight losses and reduced food consumption were observed at 700 and 500 mg/kg throughout treatment. Post-mortem findings affecting the stomach were the primary observations for these animals.
The only fetal effects were external malformations in 2 fetuses from 1

control litter.
Maternal toxicity (mortality) was evident at 500 and 700 mg/kg/day. No developmental toxicity was exhibited at any dose (50, 250 and 500 mg/kg/day).

Reliability : (1) valid without restriction
11.12.2003 (25)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : gestation days 6 through 18
Frequency of treatment : daily
Duration of test : to gestation day 29
Doses : 25, 75, 150 and 350 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL Maternalt. : = 150 mg/kg bw
NOAEL Teratogen : = 350 mg/kg bw
Method : EPA OTS 798.4900
Year : 1987
GLP : yes
Test substance : other TS: Dibromostyrene, 1770-014-07, -08 and -09.
Method : The potential maternal and developmental toxicity of Dibromostyrene were evaluated in rabbits. Dibromostyrene in corn oil was administered by gavage to four groups of 20 inseminated rabbits as a single daily dose of 25, 75, 150 and 350 mg/kg from days 6 through 18 of gestation. Twenty control females were dosed concurrently with corn oil on a comparable regimen. All surviving females were sacrificed for a Cesarean section on day 29 of gestation.
Remark : Sponsor: Great Lakes Chemical Corp. and General Electric Co.
Result : Three deaths, which were considered treatment related, had occurred at 350 mg/kg by gestation day 21. Principal clinical signs of toxicity at 350 mg/kg consisted of decreased defecation, black feces and anuria. Group mean body weight losses or reduced mean body weight gains and decreased food consumption occurred at this dose throughout treatment but were most notable in the first six days of administration. No other treatment related findings were observed. Fetal malformations observed were considered spontaneous in origin. No treatment related fetal developmental variations were observed.
Maternal toxicity (mortality, clinical signs, body weight losses and decreased food consumption) was evident at 350 mg/kg/day. No developmental toxicity was exhibited at any dose. The NOAEL for maternal toxicity was 150 mg/kg/day and for developmental toxicity was 350 mg/kg/day.

Reliability : (1) valid without restriction
11.12.2003 (24)

Species : rat
Sex : female
Strain : other: Crl:CD(R)BR
Route of admin. : gavage
Exposure period : Gestation days 6 through 15
Frequency of treatment : daily
Duration of test : Gestation day 20
Doses : 100, 200, 400, 800 and 1600 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL Maternalt. : = 400 mg/kg bw
NOAEL Teratogen : = 800 mg/kg bw
Method : EPA OTS 798.4900
Year : 1987

GLP	:	yes
Test substance	:	other TS: Dibromostyrene, 1770-014-06.
Method	:	The potential maternal and developmental toxicity of Dibromostyrene were evaluated in rats. Dibromostyrene in corn oil was administered by gavage to five groups of 10 bred rats as a single daily dose of 100, 200, 400, 800 and 1600 mg/kg from days 6 through 15 of gestation. Ten control females were dosed concurrently with corn oil on a comparable regimen. All surviving females were sacrificed for a Cesarean section on day 20 of gestation.
Remark	:	Sponsor: Great Lakes Chemical Corp. and General Electric Co.
Result	:	Survival was 100%. The only signs of maternal toxicity (clinical observations and a dose related inhibition of body weight gain and food consumption) were noted at 800 and 1600 mg/kg. The only possible indication of a developmental effect was a slightly reduced mean fetal body weight at 1600 mg/kg. Two fetuses from this group (1 litter) had unilateral microphthalmia and four fetuses (1 litter) from 200 mg/kg had multiple cranio-facial defects.
Reliability	:	(1) valid without restriction

11.12.2003 (26)

Species	:	rat
Sex	:	female
Strain	:	other: Crl:CD(R)BR
Route of admin.	:	gavage
Exposure period	:	Gestation day 6 through 15
Frequency of treatment	:	daily
Duration of test	:	Gestation day 20
Doses	:	100, 400, 800 and 1600 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL Maternalt.	:	< 100 mg/kg bw
NOAEL Teratogen	:	= 100 mg/kg bw
Method	:	EPA OTS 798.4900
Year	:	1987
GLP	:	yes
Test substance	:	other TS: Dibromostyrene, 1770-014-07, -08 and -09.
Method	:	The potential maternal and developmental toxicity of Dibromostyrene were evaluated in rats. Dibromostyrene in corn oil was administered by gavage to four groups of 25 bred rats as a single daily dose of 100, 400, 800 and 1600 mg/kg from days 6 through 15 of gestation. Twenty-five control females were dosed concurrently with corn oil on a comparable regimen. All surviving females were sacrificed for a Cesarean section on day 20 of gestation.
Remark	:	Sponsor: Great Lakes Chemical Corp. and General Electric Co.
Result	:	Compound related mortalities (5 of 25 animals) occurred at 1600 mg/kg. Clinical signs were noted at 400 mg/kg and higher. No treatment related clinical signs were observed at 100 mg/kg. Body weight gain was inhibited (not statistically significant) at 100 mg/kg during the first three days of dosing, at 400 and 800 mg/kg during the first six days of dosing and at 1600 mg/kg throughout dosing. Food consumption was significantly inhibited in all treated groups in a dose related manner during the first six days of dosing. Treatment related gross necropsy findings (2 animals that died or were moribund, 1600 mg/kg group) included dark red adrenal glands and dark red contents in the urinary bladder. Adverse effects on the developing fetus (reduced body weight and increase in post-implantation loss) were noted at 1600 mg/kg. An effect on fetal morphological development was noted at 400, 800 and 1600 mg/kg. External malformations (cranio-facial defects, primarily anophthalmia and/or microphthalmia) were noted at 1600 mg/kg. Developmental variations (unossification of sternebrae #5 and/or #6 and 7th cervical ribs) were noted at 800 and 1600 mg/kg and a slight increase in 7th cervical ribs

was noted at 400 mg/kg.
Maternal toxicity (reduced body weight gains and food consumption) was noted at all doses. Developmental toxicity was noted at doses of 400 mg/kg and higher. The NOAEL for fetal developmental toxicity was 100 mg/kg/day.

Reliability : (1) valid without restriction
11.12.2003 (24)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

6. References

(1) Wildlife International, Ltd., Project Number 298C-132, November 13, 2003.

(2) Wildlife International, Ltd., Project Number 298C-133, November 21, 2003.

(3) Wildlife International, Ltd., Project Number 298C-134, November 13, 2003.

(4) Great Lakes Chemical Corporation

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(6) Microbiological Associates, Inc, #T5283.332, March 6, 1987.

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(9) Pharmakon Research International, Inc., PH 320-GL-001-87, May, 1987.

(10) Pharmakon Research International, Inc., PH 320-GL-002-87, June, 1987.

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(12) Raltech Scientific Services, lab #800832, Jan, 1981.

(13) WIL Research Laboratories, Inc., WIL-12007, April, 1983.

(14) WIL Research Laboratories, Inc., WIL-12008, March, 1983.

(15) WIL Research Laboratories, Inc., WIL-12009, Feb., 1983.

(16) WIL Research Laboratories, Inc., WIL-12010, July, 1983.

(17) WIL Research Laboratories, Inc., WIL-12082, Jan. 29, 1987.

(18) WIL Research Laboratories, Inc., WIL-12083, June 4, 1987.

(19) WIL Research Laboratories, Inc., WIL-12084, Mar. 6, 1989.

(20) WIL Research Laboratories, Inc., WIL-12110, April 27, 1987.

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(22) WIL Research Laboratories, Inc., WIL-12112, Dec. 30, 1987.

(23) WIL Research Laboratories, Inc., WIL-12194, Nov. 12, 1993.

(24) WIL Research Laboratories, Inc., WIL-12195, Dec. 17, 1993.

(25) WIL Research Laboratories, Inc., WIL-12196, Jan. 6, 1994.

(26) WIL Research Laboratories, Inc., WIL-12198, Dec. 13, 1992.

(27) Wildlife International, Ltd., Project Number 298C-130, November 13, 2003.

(28) Wildlife International, Ltd., Project Number 298C-131, November 13, 2003.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT